Appendix A: Pending Claims

1. (Amended) An apparatus for electrical detection of molecular interactions between immobilized probe molecules and target molecules in a sample solution, comprising:

(a) a supporting substrate comprising an array of test sites,

(b) a plurality of porous, polymeric pads in contact with the supporting substrate at the test sites,

(c) a set of input electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each input electrode is arranged such that a first portion of the input electrode is in contact with a test site and a second portion of the input electrode is in contact with a different test site,

(d) a set of output electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each output electrode is arranged such that a first portion of the output electrode is in contact with a test site and a second portion of the output electrode is in contact with a different test site, and wherein each output electrode is in electrochemical contact with an input electrode,

(e) a plurality of linker moieties in contact with the porous, polymeric pads at the test sites,

(f) a plurality of probe molecules immobilized to the linker moieties, wherein said probe molecules specifically bind to or interact with target molecules,

(g) a signal generator for producing an electrical signal at each input electrode,

(h) a detector for detecting changes in the electrical signal at each output electrode, and

(i) an electrolyte solution in contact with the porous polymeric pads, input electrodes, output electrodes, linker moieties, and probe molecules, wherein molecular interactions between the immobilized probe molecules and target molecules are detected as a difference in the electrical signal detected at each output electrode in the presence and absence of target molecules.

2. (Amended) An apparatus for electrical or electrochemical detection of molecular interactions between immobilized probe molecules and target molecules in a sample solution, comprising:

(a) a supporting substrate comprising an array of test sites,

(b) a plurality of porous, polymeric pads in contact with the supporting substrate at the test sites,

(c) a set of input electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each input electrode is arranged such that a first portion of the input electrode is in contact with a test site and a second portion of the input electrode is in contact with a different test site,

(d) a set of output electrodes in contact with the plurality of porous, polymeric pads at the test sites, wherein each output electrode is arranged such that a first portion of the output electrode is in contact with a test site and a second portion of the output electrode is in contact with a different test site, and wherein each output electrode is in electrochemical contact with an input electrode,

(e) a plurality of linker moieties in contact with the porous, polymeric pads at the test sites,

(f) a plurality of probe molecules immobilized to the linker moieties, wherein said probe molecules specifically bind to or interact with target molecules,

(g) at least one reference electrode in electrochemical contact with the input and output electrodes,

(h) a signal generator for producing an electrical signal at each input electrode,

(i) a detector for detecting changes in the electrical signal at each output electrode, and

(j) an electrolyte solution in contact with the porous polymeric pads, input electrodes, output electrodes, linker moieties, reference electrode, and probe molecules, wherein molecular interactions between the immobilized probe molecules and target molecules are detected as a difference in the electrical signal detected at each output electrode in the presence and absence of target molecules.

3. (Amended) An apparatus according to claim 1, wherein the output electrodes and input electrodes are interdigitated at the test site.

4. (Amended) An apparatus according to claim 2, wherein the output electrodes and input electrodes are interdigitated at the test site.

5. The apparatus of any of Claims 1, 2, 3, or 4, wherein the supporting substrate comprises ceramic, glass, silicon, silicon nitride, fabric, rubber, plastic, printed circuit board, compound semiconductors, or combination thereof.

6. The apparatus of either Claims 1 or 2, wherein the potous, polymeric pads comprise polyacrylamide gel, agarose gel, polyethylene glycol, cellulose gel, sol gel, polypyrrole, carbon, carbides, oxides, nitrides, or combination thereof.

7. The apparatus of Claim 6, wherein the porous, polymeric pads comprise polyacrylamide gel.

8. The apparatus of any of Claims 1, 2, 3, or 4, wherein the input electrodes comprise solid or porous gold, silver, platinum, copper, titanium, chromium, or aluminum, or metal oxide, metal nitride, metal carbide, carbon, graphite, conductive plastic, metal impregnated 15 polymers, or combinations thereof.

9. The apparatus of Claim 8, wherein the input electrodes comprise platinum.

10. The apparatus of Claim 8, wherein the input electrodes comprise gold.

11. The apparatus of any of Claims 1, 2, 3, or 4, wherein the input electrodes comprise a conductive material and an insulating material.

12. The apparatus of Claim 11, wherein the conductive material is solid or porous gold, silver, platinum, copper, titanium, chromium, or aluminum, or metal oxide, metal nitride, metal carbide, carbon, graphite, conductive plastic, metal impregnated polymers, or combinations thereof.

13. The apparatus of Claim 12, wherein the conductive material is platinum.

14. The apparatus of Claim 12, wherein the conductive material is gold.

15. The apparatus of Claim 11, wherein the insulating material is glass, silicon, plastic, rubber, fabric, ceramic, printed circuit board, or combinations thereof.

16. The apparatus of Claim 15, wherein the insulating material is silicon.

17. The apparatus of Claim 15, wherein the insulating material is glass.

18. The apparatus of Claim 11, wherein the conductive material is embedded in the 10 supporting substrate and the supporting substrate comprises the insulating material.

19. The apparatus of either Claims 1 or 2, wherein a portion of each input electrode is embedded in the porous, polymeric pads at the test sites addressed by said input electrode.

20. The apparatus of any of Claims 1, 2, 3, or 4, wherein the output electrodes comprises solid or porous gold, silver, platinum, copper, titanium, chromium, or aluminum, or metal oxide, metal nitride, metal carbide, carbon, graphite, conductive plastic, metal impregnated polymers, or combinations thereof.

21. The apparatus of Claim 20, wherein the output electrode comprises platinum.

22. The apparatus of Claim 20, wherein the output electrode comprises gold.

23. The apparatus of any of Claims 1, 2, 3, or 4, wherein the output electrode comprises a conductive material and an insulating material.

24. The apparatus of Claim 23, wherein the conductive material is solid or porous gold, silver, platinum, copper, titanium, chromium, or aluminum, or metal oxide, metal nitride, metal carbide, carbon, graphite, conductive plastic, metal impregnated polymers, or combinations thereof.

25. The apparatus of Claim 24, wherein the conductive material is platinum.

26. The apparatus of Claim 24, wherein the conductive material is gold.

27. The apparatus of Claim 23, wherein the insulating matetial is glass, silicon, plastic, rubber, fabric, ceramic, printed circuit board, or combinations thereof.

28. The apparatus of Claim 27, wherein the insulating material is silicon.

29. The apparatus of Claim 27, wherein the insulating material is glass.

30. The apparatus of Claim 23, wherein the conductive material is embedded in the supporting substrate and the supporting substrate comprises the insulating material.

31. The apparatus of either Claims 1 or 2, wherein a portion of each output electrode is embedded in the porous, polymeric pads at the test sites addressed by said output electrode.

32. The apparatus of Claim 31, wherein the output electrodes and input electrodes are interdigitated at the test site.

33. The apparatus of any of Claims 1, 2, 3, or 4, wherein the linker moieties comprise a conjugated polymer or copolymer film.

34. The apparatus of Claim 33, wherein the conjugated polymer or copolymer film is polypyrrole, polythiphene, polyaniline, polyfuran, polypyridine, polycarbazole, polyphenylene, poly(phenylenvinylene), polyfluorene, or polyindole, or their derivatives, copolymers, or combinations thereof.

35. The apparatus of any of Claims 1, 2, 3, or 4, wherein the linker moieties comprise a neutral pyrrole matrix.

36. The apparatus of any of Claims 1, 2, 3, or 4, wherein the linker moieties comprise thiol linkers.

37. The apparatus of any of Claims 1, 2, 3, or 4, wherein the probe molecules are oligonucleotides or nucleic acids.

38. The apparatus of Claim 37, wherein the probe molecules are aptamers.

39. The apparatus of any of Claims 1, 2, 3, or 4, wherein the probe molecules are proteins or peptides.

40. The apparatus of Claim 39, wherein the peptides are antibodies.

41. The apparatus of Claim 40, wherem the antibodies are a polyclonal antisera, polyclonal antibodies, or F(ab), F(ab)', $F(ab)_2$,or F_v fragments thereof.

42. The apparatus of Claim 40, wherein the antibodies are monoclonal antibodies, or F(ab), F(ab)', $F(ab)_2$,or F_v fragments thereof.

43. The apparatus of Claim 40, wherein the antibodies are F(ab) fragments or single chain F_v fragments produced by in vitro libraries.

44. The apparatus of any of Claims 1, 2, 3, or 4, wherein the probe molecules comprise a natural products library, a phage display library, or a combinatorial library.

45. The apparatus of any of Claims 1, 2, 3, or 4, wherein the linker moieties comprise streptavidin and the probe molecules are biotinylated.

46. The apparatus of either Claims 1 or 2, wherein the probe molecules are first covalently linked to the linker moieties and then the linker moieties are placed in contact with the porous, polymeric pads.

47. The apparatus of either Claims 3 or 4, wherein the probe molecules are first covalently linked to the linker moieties and then the linker moieties are placed in contact with either the input electrodes, the output electrodes, or both the input electrodes and output electrodes.

48. The apparatus of either Claims 1 or 2, wherein the probe molecules are first covalently linked to the linker moieties, the linker moieties are mixed with porous, polymeric pad constituents, and then the porous, polymeric pads are polymerized.

49. The apparatus of either Claims 2 or 4, wherein the reference electrode comprises solid or porous gold, silver, platinum, copper, titanium, chromium, or aluminum, or metal oxide, metal nitride, metal carbide, carbon, graphite, conductive plastic, metal impregnated polymers, or combinations thereof.

50. The apparatus of Claim 49, wherein the reference electrode comprises platinum.

51. The apparatus of Claim 49, wherein the reference electrode comprises gold.

52. The apparatus of either Claims 2 or 4, wherein the conductive material is silver/silver chloride.

53. The apparatus of either Claims 2 or 4, wherein the reference electrode comprises a conductive material and an insulating material.

54. The apparatus of Claim 53, wherein the conductive material is solid or porous gold, silver, platinum, copper, titanium, chromium, or aluminum, or metal oxide, metal nitride, metal carbide, carbon, graphite, conductive plastic, metal impregnated polymers, or combinations thereof.

55. The apparatus of Claim 54, wherein the conductive material is platinum.

56. The apparatus of Claim 54, wherein the conductive material is gold.

57. The apparatus of Claim 53, wherein the insulating material is glass, silicon, plastic, rubber, fabric, ceramic, printed circuit board, or combinations thereof.

58. The apparatus of Claim 57, wherein the insulating material is silicon.

59. The apparatus of Claim 57, wherein the insulating material is glass.

60. The apparatus of Claim 53, wherein the conductive material is embedded in the supporting substrate and the supporting substrate comprises the insulating material.

61. The apparatus of any of Claims 1, 2, 3, or 4, wherein the supporting substrate further comprises a plurality of wells wherein each well encompasses a porous, polymeric pad, wherein a plurality of probe molecules is immobilized to linker moieties that are in contact with the porous, polymeric pad; an input electrode; and an output electrode.

62. The apparatus of any of Claims 1, 2, 3, or 4, wherein the means for producing an electrical signal at each input electrode comprises a multiplexer.

63. The apparatus of any of Claims 1, 2, 3, or 4, wherein the means for detecting changes in the electrical signal at each output electrode comprises a demultiplexer.

64. (Amended) A method for the electrical detection of molecular interactions between a probe molecule immobilized at a specific test site and a target molecule in a sample solution, comprising:

(a) applying a first electrical signal at an input electrode in contact with a first set of porous, polymeric pads, wherein the first set of porous, polymeric pads comprises the porous, polymeric pad at the specific test site,

(b) detecting the first electrical signal at an output electrode in contact with a second set of porous, polymeric pads, wherein the second set of porous, polymeric pads comprises the porous, polymeric pad at the specific test site,

(c) exposing the first and second sets of porous, polymeric pads to a sample mixture containing the target molecule,

(d) applying a second electrical signal at an input electrode in contact with the first set of porous, polymeric pads,

(e) detecting the second electrical signal at an output electrode in contact with the second set of porous, polymeric pads,

(f) comparing the first electrical signal detected in step (b) with the second electrical signal detected in step (e), and

(g) determining whether the first electrical signal is different from the second electrical signal.

65. (Amended) The method of Claim 64, wherein molecular interactions between probe molecules and target molecules are detected by using an electrical or electrochemical detection method selected from the group consisting of impedance spectroscopy, cyclic voltammetry, alternating current (AC) voltammetry, pulse voltammetry, square wave voltammetry, hydrodynamic modulation voltammetry, conductance, potential step method, potentiometric measurements, amperometric measurements, and current step method.

66. (Amended) The method of Claim 64, wherein molecular interactions between probe molecules and target molecules are detected by using an electrical or electrochemical detection method that is alternating current (AC) impedance and the AC impedance is measured over a range of frequencies.

67. (Amended) The method of Claim 64, wherein molecular interactions between probe molecules and target molecules are detected by using an electrical or electrochemical detection method that is alternating current (AC) impedance and the AC impedance is measured by transient methods with AC signal perturbation superimposed upon a direct current (DC) potential applied to an electrochemical cell.

68. (Amended) The method of Claim 64, wherein molecular interactions between probe molecules and target molecules are detected by using an electrical or electrochemical detection method that is alternating current (AC) impedance and the AC impedance is measured by impedance analyzer, lockin amplifier, AC bridge, AC voltammetry, or combinations thereof.

69. The method of Claim 64, wherein the target molecules are labeled with an electrochemically-active reporter molecule prior to exposing the first and second sets of porous, polymeric pads to a sample mixture containing the target molecule.

70. The method of Claim 69, wherein the electrochemically-active reporter-molecule comprises a transition metal complex.

71. The method of Claim 70, wherein the transition metal complex further comprises a transition metal ion that is ruthenium, cobalt, iron, zinc, nickel, magnesium, or osmium.

72. The method of Claim 70, wherein the electrochemically-active reporter-labeled target molecules are labeled with electrochemical reporter groups selected from the group consisting of 1,4-benzoquinone, ferrocene, tetracyanoquinodimethane, N,N,N',N'-tetramethyl-p phenylenediamine, and tetrathiafulvalene.

73. The method of Claim 70, wherein the electrochemically-active reporter-labeled target molecules are labeled with electrochemical reporter groups selected from the group consisting of 9-aminoacridine, acridine orange, aclarubicin, daunomycin, doxorubicin, pirarubicin, ethidium bromide , ethidium monoazide , chlortetracycline, tetracycline , minocycline , 25 Hoechst 33258, Hoechst 33342, 7-aminoactinomycin D, Chromomycin A_3, mithramycin A, Vinblastine, Rifampicin, Os(bipyridine)$_2$(dipyridophenazine)$_2^+$, Co(bipyridine)$_3^{3+}$, and Fe bleomycin.

74. The method of Claim 64, wherein the first and second electrical signals are applied using a multiplexer.

75. The apparatus of Claim 64, wherein the first and second electrical signals are detected using a demultiplexer.

76. (New) The apparatus of claim 1, wherein the input and output electrodes are embedded in the porous, polymeric pads at the test sites.

77. (New) The apparatus of claim 2, wherein the input and output electrodes are embedded in the porous, polymeric pads at the test sites.

78. (New) The apparatus of claim 1, 2, 3, or 4 wherein each test site is uniquely indentified by two electrodes, a first electrode chosen from the set of input electrodes, and a second electrode chosen from the set of input electrodes.

79. (New) The apparatus of claim 78, wherein the array of test sites is x-y addressable in that each electrode in the set of input electrodes defines an x coordinate, and each electrode in the set of output electrodes defines a y coordinate.

80. (New) The apparatus of claim 78, wherein the array of test sites is x-y addressable in that each electrode in the set of output electrodes defines an x coordinate, and each electrode in the set of input electrodes defines a y coordinate.